-- Specific examples of antibodies which bind the CD20 antigen include: "Rituximab" ("RITUXAN®") (US Patent No. 5,736,137, expressly incorporated herein by reference); yttrium-[90]-labeled 2B8 murine antibody "Y2B8" (US Patent No. 5,736,B7, expressly incorporated herein by reference); murine IgG2a "B1" optionally labeled with ^{131}I, "^{131}I-B1" antibody (BEXXAR™) (US Patent No. 5,595,721, expressly incorporated herein by reference); murine monoclonal antibody "1F5" (Press *et al. Blood* 69(2):584-591 (1987); and "chimeric 2H7" antibody (US Patent No. 5,677,180, expressly incorporated herein by reference). --

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3. The paragraph beginning on page 14, line 25, is replaced with the following paragraph, in which the term "8.OnM" is rewritten:

-- The terms "rituximab" or "RITUXAN®" herein refer to the genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen and designated "C2B8" in US Patent No. 5,736,B7, expressly incorporated herein by reference. The antibody is an IgGI kappa immunoglobulin containing murine light and heavy chain variable region sequences and human constant region sequences. Rituximab has a binding affinity for the CD20 antigen of approximately 8.0 nM.-- 4

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4. The paragraph beginning on page 16, line 32, is replaced with the following paragraph, in which errors in the list of isotopes are corrected:

-- The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes *(e.* g. At-211, I-131, I-125, Y-90, Re-186, Re-l88, Sm-153, Bi-212, P-32, and radioactive isotopes of Lu), chemotherapeutic agents, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, or fragments thereof. --

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5. The paragraph beginning on page 40, line 27, is replaced with the following paragraph, in which "CD37 or CD22" is replaced with "or CD37" to avoid repitition:

-- As noted previously, the B cell depleting antibody and the immunoregulatory antibody may be in the same or in different formulations. These antagonist formulations can be administered separately or concurrently, and in either order. Preferably, the B cell depleting

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antibody specific to the B cell antigen target, *e.g.*, CD20, CD19, CD22, or CD37, will be administered separately from the immunoregulatory antibody, *e.g.*, an anti-CD40L antibody, anti-CD40 antibody, or anti-B7 antibody. Preferably, the CD40L antibody will be the humanized anti-CD40L antibody disclosed in U.S. Patent 6,001,358 and the anti-B7 antibody the primatized antibody disclosed in US Patent 6,113,898. As noted, this antibody has recently been show to possess apoptotic activity. Also the preferred CD40L antibody has been shown to have efficacy in treatment of both T and B cell autoimmune diseases. Also, unlike another humanized anti-CD40L antibody *(5c8)* reported by Biogen, this antibody is not known to cause any adverse toxicity.

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6. The paragraph beginning on page 41, line 11, is replaced with the following paragraph, in which spaces are inserted in the recited dosages, between the numeric value and the dosage unit:

-- The preferred B cell depleting antibody is RITUXAN®. Suitable dosages for such antibody are, for example, in the range from about 20 mg/m^2 to about 1000 mg/m^2. The dosage of the antibody may be the same or different from that presently recommended for RITUXAN® for the treatment of non-Hodgkin's lymphoma. For example, one may administer to the patient one or more doses of substantially less than 375 mg/m^2 of the antibody, *e.g.* where the dose is in the range from about 20 mg/m^2 to about 250 mg/m^2, for example from about 50 mg/m^2 to about 200 mg/m^2. --

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7. The paragraph beginning on page 41, line 19, is replaced with the following paragraph, in which spaces are inserted in the recited dosages, between the numeric value and the dosage unit:

-- Moreover, one may administer one or more initial doses) of the antibody followed by one or more subsequent dose(s), wherein the mg/m^2 dose of the antibody in the subsequent doses) exceeds the mg/m^2 dose of the antibody in the initial dose(s). For example, the initial dose may be in the range from about 20 mg/m^2 to about 250 mg/m^2 *(e.g.* from about 50 mg/m^2 to about 200 mg/m^2) and the subsequent dose may be in the range from about 250 mg/m^2 to about 1000 mg/m^2. --

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8. The paragraph beginning on page 46, line 16, is replaced with the following paragraph, in which "CD40L" is replaced with "sCD40L" in accord with the description of soluble CD40L (sCD40L) in lines 19-25 of the same page:

-- Fig. 2A shows the effect of an anti-CD40L antibody (IDEC-131) on CD40L-CD40 mediated resistance of DHL-4 cells to cell death induced by ADM. DHL-4 cells (0.5×10^6 cells/ml) were incubated in the presence of 10 μg/ml of soluble CD40L (sCD40L, P. A. Brams, E. A. Padlan, K. Hariharan, K. Slater, J. Leonard, R. Noelle, and R. Newman, "A humanized anti-human CD 154 monoclonal antibody blocks CD 154-CD40 mediated human B cell activation," *(manuscript submitted)*) for 1 hour at 37°C. After 1 hour of incubation, low concentrations of ADM (2×10^{-7} M - 4×10^{-8} M) were added and incubated for another 4 hours in the presence or absence of sCD40L (10 μg/ml). Following exposure to ADM, cells were washed and resuspended in growth medium at 0.5×10^6 cells/ml concentration, and 100 μl of cell suspension added to each well of 96-well flat bottom plate, in duplicate, with or without sCD40L. sCD40L (10 μg/ml) was added to cultures that have been continuously exposed to sCD40L during ADM treatment and to cultures that had no sCD40L during ADM exposure. In addition, IDEC-131 at 10 μg/ml was added to cultures to determine its effect on DHL-4 cells incubated with sCD40L and ADM. After 5 days, the cytotoxicity was measured by Alamar Blue dye-uptake assay, as described. --

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9. The paragraph beginning on page 47, line 6, is replaced with the following paragraph, in which the description is amended to make it clear that the control CE9.1 antibody is an anti-CD-4 antibody as noted on line 26 of page 47, and to correct misspelling of RITUXAN®:

-- The addition of IDEC-131 alone had no effect on DHL-4 cells treated with sCD40L, which indicates that the antibody, by itself, does not have any direct inhibitory or cytotoxic activities on DHL-4 cells (**Fig. 2B**). DHL-4 cells pre-incubated with and without sCD40L were cultured in the presence of different concentrations of IDEC-131, RITUXAN®, the anti-CD20 antibody, and CE9.1, an anti-CD4 antibody (Anderson et al., *Clin. Immunol. & Immunopathol.* 84: 73-84 (1997)). After 5 days, the cytotoxicity/proliferation of DHL-4 cells was determined by Alamar Blue assay, as described above. **Fig. 2B** shows no effect on the proliferation or the cytotoxicity of DHL-4 cells by IDEC-131, whereas RITUXAN®, as

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a9 expected, inhibited cell proliferation and induced cytotoxicity. No effect was seen in the DHL-4 cells cultured with anti-CD4 antibodies. --

10. The paragraph beginning on page 49, line 6, is replaced with the following paragraph, is amended to more clearly identify the composition and source of the trademarked product Dynabeads™ , in accord with the requirements of the official action:

– To determine the effect of IDEC-131 on the growth and survival of B-CLL cells *in vitro*, B-CLL cells were cultured with and without IDEC-131 in the presence of CD40L *in vitro*. Peripheral blood mononuclear cells (PBMC) were isolated from a CLL patient's blood using a Ficoll-Hypaque gradient centrifugation. Viability was determined by Trypan blue dye exclusion and was >98%. Flow cytometric analysis revealed that >70% of the lymphocytes were CD 19^+/$CD20^+$. CLL cells (PBMC) were cultured in CLL growth medium (e.g., RPMI-1640 medium supplemented with

a10 5% FCS or 2% of autologous donor plasma, supplemented with 2 mM L-Glutamine and 100 U/ml Penicillin-Streptomycin). In addition, for some experiments, $CD19^+$ B-cells were purified using $CD19^+$ Dynabeads™ (uniform, 4.5 μm, magnetizable polystyrene beads coated with a primary monoclonal antibody specific for CD4) as per manufacturer's instructions (Dynal, Oslo, Norway, Cat. #111.03/ 111.04) and cultured as above. CLL or purified B-CLL cells cultured in growth medium mostly under went spontaneous apoptotic cell death. However, culturing these cells in the presence of sCD40L extended their viability in cultures. **Table II** indicates the cell viability of CD 19^+ B-CLL cells grown in the presence or absence of sCD40L (5 μg/ml) at different time points and indicates the longer survival of CLL cells. B-CLL cells from Patient #1 cultured with sCD40L had ≥ 60% viability for greater than 2 weeks, whereas cells grown in the absence of sCD40L had less than 10% viability. --